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EXAMINER

PRATS, FRANCISCO CHANDLER

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1651

DATE MAILED: 04/23/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/720,041

Applicant(s)

SCHLOTHAUER ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-36, 39-50, 59 and 62-68 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-36, 39-50, 59 and 62-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The amendment filed February 26, 2003 (certificate of mailing February 21, 2003), has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 37, 38, 51-58, 60 and 61 have been cancelled.

Claims 63-68 have been added.

Claims 32-36, 39-50, 59 and 62-68 are pending and are examined on the merits.

Specification

The amendment filed February 26, 2003, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the recitation in the claims and specification of "conditions which produce a hydrolysate with a solubility of at least 65%."

While applicant alleges support in the specification as originally filed, originally filed pages 3 and 4 of the specification mention nothing about a limitation requiring the hydrolysate to have at least 65% solubility. It is noted that

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Example 4 on page 10 of the as-filed specification, as opposed to Example 5, states that the solubility of various whey hydrolysates are 65%, 70% and 85%. Thus, while the originally filed specification may support a limitation of 65% to 85%, the language "at least 65%" encompasses solubilities of up to 100%, which are clearly not disclosed or contemplated by the as-filed specification. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

Claims 32-36, 39-50, 59 and 62-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As amended, the claims now recite the additional step of testing the whey hydrolysate for "bio-activity." This new claim language encompasses testing for many biological activities, for example anti-AIDS activity, which are clearly not supported by the disclosure as filed. Rather, the only "bioactivities" disclosed in the specification as filed are angiotensin converting enzyme inhibition and a taste test for bitterness. This is a new matter rejection.

Also, as discussed above with respect to the specification, claim 32 now recites the limitation of a hydrolysis under "conditions which produce a hydrolysate with a solubility of at least 65%." As pointed out above, while the originally filed specification may support a limitation of 65% to 85% solubility, the language "at least 65%" encompasses solubilities of up to 100%, which are clearly not disclosed or contemplated by the as-filed specification.

Claim Rejections - 35 USC § 112

Claims 32-36, 39-50, 59 and 62-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As amended, claim 32 requires the hydrolysate to have a solubility of 65%. However, the claim fails to state what solvent must be used to determine the solubility. The metes and bounds of the new solubility limitation are therefore not clear. Claim 32 and its dependents must therefore be considered indefinite under § 112, second paragraph.

Claim Rejections - 35 USC § 102

Claims 32, 39, 45, 50 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Mellqvist et al (U.S. Pat. 4,847,096).

Mellqvist discloses a process whereby a whey protein concentrate is contacted with a protease at 50°C and pH 8 to a degree of hydrolysis of 4.1, after which the enzyme is inactivated by decreasing pH to 4 for 60 min. See Example 3, at column 4, lines 40-45. Note also Mellqvist's disclosure of suitable degrees of hydrolysis ranging from 0.2 to 4.0 (column 2, lines 7-12), clearly encompassing the claimed range of "no greater than 10%" (claim 32) and "about 4% to about 10%" claim 63.)

As amended, claim 32 and its dependents require the hydrolysate to have a solubility of 65%. This limitation is considered to be inherently met by Mellqvist. Specifically, applicant's disclosure demonstrates that if one performs the exact hydrolysis processes disclosed in Mellqvist, one achieves the claimed solubility. See Example 4 in the specification. That is, Mellqvist contacts the same substrate, whey, with the exact commercial enzyme product used by applicant, Neutrase, to achieve the exact degree of hydrolysis. Because the prior art performs the same chemical reaction disclosed by applicant as

resulting in the claimed solubility, the prior art process must also result in the claimed solubility.

Claim 32 has also been amended to require the hydrolysate to be tested for "bio-activity." Clearly, the phrase "testing . . . for bio-activity" encompasses any testing for any biological reaction to a stimulus. The hydrolysate in Examples 1 to 3 of Mellqvist is subjected to a taste test. Taste is clearly a "bio-activity" because the sensation of taste is produced by living cells reacting to a substance. The limitation requiring a test of bio-activity is clearly met by Mellqvist.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. As discussed above, the addition of a test for bio-activity to the claimed process does not distinguish the claims from Mellqvist because Mellqvist performs a taste test on several of his hydrolysates. In short, applicant's argument ignores the breadth of the recitation "testing . . . for bio-activity." The rejection must therefore be maintained.

Claim Rejections - 35 USC § 103

Claims 32-36, 39, 40, 42-44 and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mellqvist et al (U.S. Pat. 4,847,096).

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Mellqvist discloses a process of improving the taste and storage stability of whey proteins, whereby a whey protein concentrate is contacted with the claimed protease Neutrase ® at 20°C and pH 7 to a degree of hydrolysis of 1.2, after which the enzyme is inactivated by decreasing pH to 4 for 60 min. See Example 2, at column 4, lines 20-37. Example 2 of Mellqvist differs from the claims in that Mellqvist uses a temperature which is slightly lower than that claimed.

However, Mellqvist clearly discloses that temperature may be routinely varied as long as the desired degree of hydrolysis is obtained. See column 2, lines 48-55. Moreover, Mellqvist discloses generally that a degree of hydrolysis between 0.5 and 4.0 is desirable in such processes. See column 2, lines 5-12. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have been motivated to have determined process conditions suitable for performing Mellqvist's process, and would have been motivated to have performed Mellqvist's process under those process conditions process conditions, so as to produce a whey hydrolysate with a degree of hydrolysis of 4, as disclosed by Mellqvist as being desirable.

Moreover, the selection of a sweet whey starting material would have been obvious in view of Mellqvist's disclosure that virtually any whey product can be used as a starting material.

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See column 3, lines 23-31. Further still, the use of heat deactivation in Mellqvist's process, and the determination of suitable temperatures therefor, would have been obvious in view of Mellqvist's disclosure of the suitability thereof. See column 3, lines 1-6. Still further, the use of immobilized enzymes is well known in the art, and would have been obvious in view of Mellqvist's disclosure. Further still, the use of a whey substrate containing high amounts of lactose would also have been obvious, in view of Mellqvist's disclosure that virtually any whey product can be used as a starting material. See column 3, lines 23-31. A holding of obviousness over the cited claims is therefore required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant's sole argument regarding this ground of rejection is that the addition of a step of "testing . . . for bioactivity" to the claimed process renders Mellqvist inapplicable as prior art because Mellqvist does not disclose such a step. However, as discussed above, the addition of a step of testing for bio-activity to the claimed process does not distinguish the claims from Mellqvist because Mellqvist performs a taste test on several of his hydrolysates. Taste is clearly

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encompassed by the recitation "bio-activity." The rejection must be maintained.

Claims 32 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mellqvist et al (U.S. Pat. 4,847,096) in view of Shimamura et al (EP 0 799 577).

As discussed above, Mellqvist discloses and renders obvious the process recited in claim 32. Mellqvist differs from the claims in that Mellqvist does not disclose the use of ultrafiltration in the enzyme deactivation step. However, Shimamura discloses that protease inactivation by ultrafiltration is convention in processes of preparation enzymatic whey hydrolysates. See page 15, second full paragraph. Thus, the artisan of ordinary skill, recognizing from Shimamura the suitability of ultrafiltration as an enzyme-removing step in the preparation of enzymatic hydrolysates of whey, clearly would have been motivated to have used ultrafiltration in Mellqvist's process with a reasonable expectation that it would have functioned at least equivalently to the enzyme inactivation techniques disclosed by Mellqvist. Claim 41 must therefore be considered obvious over the cited references.

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All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant's sole argument regarding this ground of rejection is that the addition of a step of "testing . . . for bioactivity" to the claimed process renders Mellqvist inapplicable as prior art because Mellqvist does not disclose such a step. However, as discussed above, the addition of a step of testing for bio-activity to the claimed process does not distinguish the claims from Mellqvist because Mellqvist performs a taste test on several of his hydrolysates. Taste is clearly encompassed by the recitation "bio-activity." The rejection must be maintained.

Claims 32, 45 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mellqvist et al (U.S. Pat. 4,847,096) in view of Soehnlén (U.S. Pat. 4,358,464).

As discussed above, Mellqvist discloses and renders obvious the process recited in claim 32. Mellqvist differs from the claims in that Mellqvist does not disclose the use of β -galactosidase in treating the whey product, as recited in claims 45 and 49. However, Soehnlén discloses that the use of β -galactosidase in treating a whey product, improves the taste of the product. See abstract. Thus, the artisan of ordinary

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skill, recognizing from Soehnlén the advantage of β -galactosidase as a taste improving step in the preparation of enzymatic hydrolysates of whey, clearly would have been motivated to have used β -galactosidase in Mellqvist's process to further improve the taste of the resulting product. Claim 49 must therefore be considered obvious over the cited references.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. As is the case in the art rejections set forth above, applicant's sole argument regarding this ground of rejection is that the addition of a step of "testing . . . for bioactivity" to the claimed process renders Mellqvist inapplicable as prior art because Mellqvist does not disclose such a step. However, as discussed above, the addition of a step of testing for bioactivity to the claimed process does not distinguish the claims from Mellqvist because Mellqvist performs a taste test on several of his hydrolysates. Taste is clearly encompassed by the recitation "bio-activity." The rejection must be maintained.

Claims 32, 59 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mellqvist et al (U.S. Pat. 4,847,096) in view of Mullally (Int. Dairy Journal 7:299-303 (1997)). As

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discussed above, Mellqvist discloses and renders obvious the process recited in claim 32. Mellqvist differs from the claims in that Mellqvist does not disclose the use of the enzymatic hydrolysate produced therein in the treatment of hypertension, as recited in claim 62, or in the assays of angiotensin converting enzyme (ACE) inhibition, as recited in claims 66-68. However, Mullally clearly discloses that hydrolysates of whey produced by proteases having a variety of specificities all possess anti-hypertensive activity, and that ACE inhibition is a measure of the anti-hypertensive activity. See page 301, Table 1. Thus, in view of Mullally, the artisan of ordinary skill would have reasonably expected the enzymatic whey digests of Mellqvist to have had anti-hypertensive properties as well, and would have been motivated to have used Mellqvist's enzymatic whey digests in a treatment of hypertension, and would have been further motivated to have tested the anti-hypertensive properties of the hydrolysates by performing an ACE inhibition assays, as disclosed by Mullally.

New claims 64 and 65 require the additional step of using high performance liquid chromatography to separate the various peptides present in the whey hydrolysate. While neither Mellqvist nor Mullally disclose the use of chromatography in the separation of peptides, Mullally clearly discloses that using

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filtration to fractionate the hydrolysates on a molecular weight basis filtration results in fractions having differing, and in some cases increased, anti-hypertensive activity. Thus, Mullally clearly discloses the desirability of fractionating protease-digested whey on a molecular weight basis. The artisan of ordinary skill, recognizing at the time of applicant's invention that high performance liquid chromatography (HPLC) was a well known method of fractionating protein mixtures on the basis of molecular weight, clearly would have considered HPLC a suitable method of separating Mellqvist's whey hydrolysate on a molecular weight basis, so as to isolate those peptide fractions containing increased anti-hypertensive activity, said fractionation being taught by Mullally as being advantageous. A holding of obviousness is therefore required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. As discussed above, the addition of a bio-activity testing step does not distinguish the process of claim 32 and its dependents from Mellqvist's process. Applicant's argument regarding the product recited in claim 59 is treated below. Also, the academic nature of Mullally's disclosure is noted, as is Mullally's disclosure of enzyme inactivation by heating to 80 degrees C for 20 minutes, and the alleged insoluble proteins

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resulting therefrom. However, note specifically that Mullally is only applied to demonstrate the obviousness of the use of whey hydrolysates, such as produced by Mellqvist, in treating hypertension, and not to demonstrate the obviousness of the process of making such hydrolysates. As discussed above, it is Mellqvist which anticipates and/or obviates the claimed processes of using proteases to yield hydrolyzed whey proteins/peptides. Mullally is applied to demonstrate the obviousness using the hydrolysate to treat hypertension. Thus, applicant's argument does not address the way references are applied to the claimed limitations. The rejection must therefore be maintained.

Claim Rejections - 35 USC § 102/103

Claim 59 is rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Mellqvist et al (U.S. Pat. 4,847,096).

The reference discloses a product which appears to be identical to the presently claimed product, based on the fact that the prior art product is produced by contacting the same enzyme, Neutrase®, with the same substrate, whey, to yield a product having the same degree of hydrolysis as recited in the claims. See Example 2, at column 4, lines 20-37. Consequently,

the claimed product, including the peptide sequences, appears to be anticipated by the reference.

However, even if the reference product and the claimed product are not one and the same and there is, in fact, no anticipation, the reference product would, nevertheless, have rendered the claimed strain obvious to one of ordinary skill in the art at the time the claimed invention was made in view of the fact any difference between the claimed product and the prior art product would be the nominal difference expected, due to variations in starting materials and in differing batches of enzymes and starting materials. Thus the claimed invention as a whole was clearly *prima facie* obvious especially in the absence of sufficient, clear, and convincing evidence to the contrary.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant states that Mellqvist does not disclose any of the peptides recited in claim 59. However, applicant's argument is simply not supported by any fact currently of record. Claim 59 recites "any combination of two or more" of a list of ten peptides. Applicant's specification clearly discloses that when a whey-containing substrate is hydrolyzed with the protease Neutrase ® to a degree of hydrolysis of less than 10%, the result is a combination of peptides as recited in claim 59.

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See, e.g., Examples 3 and 15. Because Mellqvist performs the exact process disclosed by applicant as resulting the combination of peptides recited in claim 59, Mellqvist discloses the combination of peptides recited in claim 59. While it is conceded that the reference's disclosure of the claimed product is inherent rather than explicit, the reference must nonetheless be considered at least anticipatory. If Mellqvist does not disclose the claimed product then applicant's disclosure must be considered non-enabling.

In sum, on the current record it appears that identical starting materials are contacted with an enzyme which catalyzes the identical chemical reaction, to result in an identical product. Indeed, the prior art enzyme is the very same commercial product as disclosed in the specification. The evidence for anticipation, both regarding structure and method of making is overwhelming. Significantly, applicant provides no factual evidence whatsoever to refute the holding of anticipation. Note specifically that on the current record the only way of overcoming such a clear holding of anticipation is factual proof that the rejection is in error. See MPEP § 2112, disclosing that once a proper holding of anticipation is made, the burden shifts to applicant to demonstrate an unobvious difference between the claims and the prior art. See also, In

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re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) ("the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product"). Because applicant has not demonstrated any difference between the claimed products and the prior art products, the rejection of record clearly must be maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated

from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
April 18, 2003